United States
Environmental Protection
Agency

Office of Prevention, Pesticides
and Toxic Substances
(7501C)

Pesticide Fact Sheet

Name of Chemical: Fluthiacet-methyl
Reason for Issuance: Conditional Registration
Date Issued: April 1999

DESCRIPTION OF CHEMICAL

Generic Name: acetic acid[[2-chloro-4-fluoro-5-[(tetrahydro-3-oxo-1*H*,3*H*-[1,3,4]thiadiazolo[3,4-α]pyridazin-1-ylidene)amino]phenyl]thio]-methyl ester

Common Name: Fluthiacet-methyl

Trade Names: Fluthiacet-Methyl Technical
Action Herbicide

EPA Chemical Code: 108803

Chemical Abstracts Service (CAS) Number: 117337-19-6

Year of Initial Registration: 1999

Pesticide Type: Herbicide

Chemical Family: Imine chemical

U.S. and Foreign Producers: Novartis Crop Protection, Inc.
P.O. Box 18300
Greensboro, NC 27419

USE PATTERNS AND FORMULATIONS

Fluthiacet-methyl is applied to actively growing weeds in soybeans to control annual broadleaf weeds, and is particularly effective in controlling velvetleaf. It will be formulated as a 4.75% wettable powder in water-soluble bags [Action Herbicide]. Action Herbicide will be applied by ground application at 1.2 to 2.25 ounce per acre (A)[0.0035 to 0.0066 pounds active ingredient (ai)/A]. If second application of Action Herbicide is needed, not more than 3 ounce of Action can be applied [Equivalent to a maximum seasonal application rate of 0.0089 lb fluthiacet-methyl ai per acre per cropping season].

Fluthiacet-Methyl Technical is a 98% manufacturing use product.

SCIENCE FINDINGS

SUMMARY SCIENCE STATEMENTS

Adequate chemistry, toxicological, ecological effects, and environmental fate data have been submitted and reviewed to support the conditional registration of Action Herbicide on soybeans and Fluthiacet-Methyl Technical as a manufacturing use pesticide until March 31, 2001.

The technical fluthiacet-methyl product is classified in toxicity category III [CAUTION] based on an acute dermal toxicity study. The Action Herbicide formulated end use product is classified in toxicity category III [CAUTION] based on the acute dermal toxicity study.

An acute neurotoxicity study was negative. In a rat subchronic neurotoxicity study the systemic No Observed Adverse Effect Level (NOAEL) was 0.576 milligrams/kilogram(mg/kg)/day for males and 1,354 mg/kg/day the highest dose tested [HDT] for females. The neurotoxicity NOAEL was 20,000 ppm (1,128 and 1,354 mg/kg/day for males and females, respectively)[HDT].

Fluthiacet-methyl was negative for mutagenic/genotoxic effects in bacterial or cultured mammalian cells and did not cause DNA damage in bacterial or primary rat hepatocytes. *In vitro* cytogenetic assays performed with two different mammalian cell lines was clastogenic with and without S9 activation. Fluthiacet-methyl is negative for micronuclei induction in mouse bone marrow, but a significant increase in micronuclei is seen in stimulated rat liver cells following *in vivo* exposure.

In a rat developmental study the NOAEL for maternal toxicity and developmental toxicity is equal to or greater than 1,000

mg/kg/day [HDT]. In a rabbit developmental study, the NOAEL for maternal toxicity was 1,000 mg/kg/day [HDT] and the developmental NOAEL was 300 mg/kg/day and the Lowest Observed Adverse Effect Level (LOAEL) was 1,000 mg/kg/day based on a slight non-significant increased incidence of irregularly shaped sternebrae attributed to a delay in fetal development. In a two-generation rat reproduction study, the parental systemic NOAEL was 1.59 mg/kg/day and for males and 1.73 mg/kg/day for females. The reproductive NOAEL was 31.8 mg/kg/day for males and 37.1 mg/kg/day for females and the reproductive LOAEL was 313 mg/kg/day for males and 388 mg/kg/day for females based on decreases in mean litter body weights.

In a 90-day rat feeding study the NOAEL was 6.19 mg/kg/day for males and 6.80 mg/kg/day for females. In a 6-week dog dietary study the NOAEL was 236 mg/kg/day for males and 77.7 mg/kg/day for females. In a 28-day rat dermal study the NOAEL was 1000 mg/kg/day [HDT]. In a 1-year dog chronic feeding study, the NOAEL was 57.6 mg/kg/day for males and 30.3 mg/kg/day for females and the Lowest Observed Adverse Effect Level (LOAEL) was 582 mg/kg/day for males and 145 mg/kg/day for females based on effects observed in the erythropoietic system and the liver.

In the rat chronic feeding/carcinogenicity study the systemic toxicity NOAEL was 2.1 mg/kg/day in males and 2.5 mg/kg/day in females and the systemic toxicity LOAEL was 130 mg/kg/day in males and 154 mg/kg/day in females based on decreased body weights, liver toxicity, pancreatic toxicity and microcytic anemia in males; and liver toxicity, uterine toxicity and slight microcytic anemia in females. In males only at 130 and 219 mg/kg/day, respectively, there was an increase in the trend toward pancreatic exocrine adenomas and pancreatic islet cell adenomas.

In the mouse carcinogenicity study the systemic toxicity NOAEL was 0.1 mg/kg/day in males and females and the systemic toxicity LOAEL was 1.0 mg/kg/day in males and 1.2 mg/kg/day in females based on non-neoplastic liver findings. In males at 10 and 32 mg/kg/day, respectively, there was an increase in the number of mice with hepatocellular adenomas, carcinomas and/or adenomas/carcinomas.

Fluthiacet-methyl is classified as a "likely to be a human carcinogen" based on the presence of pancreatic tumors (exocrine adenomas, islet cell adenomas and combined islet cell adenomas + carcinomas) in male rats and liver tumors (adenomas and combined adenomas + carcinomas) in male and female mice.

Based on the results of the rat metabolism studies, fluthiacet-methyl was absorbed rapidly at both the low and high dose for both male and female rats. Repeated oral dosing had no effect on extent of absorption. Tissue levels of ^{14}C-fluthiacet-methyl derived radioactivity in the single and repeated low dose groups did not exceed 0.018 ppm for any tissue. At the single high dose, female rats showed higher levels of ^{14}C-fluthiacet-methyl derived radioactivity in tissues than males except for muscle, brain, fat and plasma. Excretion in males was predominantly in feces for all dose groups, with between 67-87% of administered radioactivity excreted by this route. In females, the percentage of administered radioactivity in urine across all dose groups (40-48%) was approximately equivalent to the percent excreted in feces (39-52%). The greater fecal excretion in males was based on a greater percentage excretion in bile for males (37%) vs. females (19%).

Based on fluthiacet-methyl's low toxicity, acute- and short- and intermediate term dietary risk assessments are not needed.

The chronic Reference Dose (RfD) for fluthiacet-methyl is 0.001 mg/kg/day. This value is based on the systemic NOAEL of 0.1 mg/kg/day in the mouse carcinogenicity study with a 100-fold uncertainty factor to account for interspecies extrapolation (10x) and intraspecies variability (10x).

A DEEM chronic exposure analysis was conducted using tolerance levels for soybeans and assuming that 25 percent of the crop is treated to estimate dietary exposure for the general population and 22 subgroups. The chronic analysis showed that exposures from tolerance level residues in or on soybeans for non-nursing infants less than 1 years old (the subgroup with the highest exposure) would be 0.6% of the chronic Reference Dose (RfD). The exposure for the general U.S. population would be less than 0.1% of the chronic RfD.

A lifetime dietary carcinogenicity exposure analysis was conducted for fluthiacet-methyl using the proposed tolerances along with the assumption of 25% of the crop treated and a Q* of 2.07×10^{-1} $(mg/kg/day)^{-1}$. A lifetime risk exposure analysis was also conducted using the DEEM computer analysis. The estimated cancer risk (2.06×10^{-7}) is less than the level that the Agency usually considers for negligible cancer risk estimates.

A cancer occupational risk assessment was conducted and the base line total risk for occupational exposure was calculated to range from 6.6×10^{-7} to 6.5×10^{-8}. This is a level which the Agency generally considers to be acceptable for excess life-time

occupational cancer risk.

The drinking water level of comparisons (DWLOCs) for chronic exposure to fluthiacet-methyl in drinking water calculated for U.S. population was 35 ppb and for non-nursing infants less than 1 year old the DWLOC was 10 ppb. EPA's chronic drinking water level of comparison for the U.S. population and the subgroup of concern is above the estimated exposures (Drinking Water Estimated Concentrations [DWECs]) for fluthiacet-methyl in water of 0.3 ppb for surface water and 0.002 ppb for groundwater.

A DWLOC for cancer was calculated as 0.133 ppb. The DWEC in surface water and groundwater for fluthiacet-methyl are 0.1 ppb [0.3 ppb(the 56-day concentration)/3] and 0.002 ppb, respectively. The model exposure estimates are less than the cancer DWLOC.

EPA concludes that there is a reasonable certainty that no harm will result from aggregate exposure to fluthiacet-methyl residues. The nature of the residue in plants is adequately understood for the purposes of this tolerance. Based on the results of animal metabolism studies, it is unlikely that significant residues would occur in secondary animal commodities from this use.

Tolerances are established for residues of the herbicide, fluthiacet-methyl, acetic acid, [[2-chloro-4-fluoro-5-[(tetrahydro-3-oxo-1*H*,3*H*-[1,3,4]thiadiazolo[3,4-α]pyridazin-1-ylidene)amino]phenyl]thio]-methyl ester, in or on soybeans at 0.01 part per million (ppm).

Fluthiacet-methyl in combination with its free acid equivalent was effectively stable against simple hydrolysis. Parent fluthiacet-methyl and three degradates are not persistent to photodegradation in water with combined half-life to be 9.5 and 13.4 days respectively in two studies. On soil surfaces, parent fluthiacet-methyl and three degradates photolyzed with a half-life of 12.4 days.

Parent fluthiacet-methyl and three degradates in aerobic soil degraded with a combined half-life of approximately 8 ± 3 days and 7 ± 4 days, respectively in two studies. Parent fluthiacet-methyl and three degradates in anaerobic soil degraded with a combined half-life of approximately 10 ± 4 days in two studies.

Fluthiacet-methyl was determined to be very mobile in soils. Parent fluthiacet-methyl and three degradates had an effective or combined half-life of approximately 6 days. Although mobile, the

transience of parent fluthiacet-methyl and its degradates means that the environmental exposure times and exposure concentrations relative to toxicity would be low.

Fluthiacet-methyl per se did not bioconcentrate in bluegill sunfish but numerous structurally related transformation products were identified. All residues combined in fish tissue were 20x, 450x and 300x for edible tissue, nonedible tissue and whole fish respectively.

Based on GENEEC and SCI-GROW computer models, the estimated drinking water concentrations (DWECs) of fluthiacet-methyl in surface water and ground water are expected to be 0.3 µg/L and 0.002 µg/L, respectively.

Fluthiacet-methyl was shown to be practically non-toxic to birds, practically non-toxic to small mammals, practically non-toxic to bees and other beneficial insects, very highly toxic to fish, and moderately toxic to fresh water invertebrates. Environmental Hazard Precautionary Statements are required.

There are no acute or chronic risk to non-target endangered fish, birds, aquatic invertebrates, terrestrial or aquatic plants or endangered species. Risks to endangered terrestrial and aquatic species are expected to be minimal from the use of Action Herbicide on soybeans. Because surfactant is used with the end-use product, and may enhance the product's phytotoxicity, limited vegetative vigor test with onion, tomato, cucumber and an aquatic test with duckweed are a condition of the registration for Action Herbicide.

TECHNICAL CHEMICAL CHARACTERISTICS

Empirical Formula:	$C_{15}H_{15}N_3O_3ClFS_2$
Molecular Weight:	403.9
Color:	Off-white with yellow tint
Physical State:	Solid powder
Odor:	Odorless
Melting Point:	105 - 106.5°C with decomposition

Density: 0.43 g/cm^3 at 20°C

Solubility: water - 0.85 µg/L (at 25°C)
0.78 µg/L (pH 5 and 7)
0.22 µg/L (pH 9)
acetone - 10.1 g/L
acetonitrile 6.87 g/L
dichloromethane - 53.1 g/L
ethyl acetate 7.35 g/L
n-hexane - 0.0232 g/L
n-octanol - 0.186 g/L
methanol - 0.441 g/L
toluene - 8.40 g/L

Vapor Pressure: 3.31 x 10^{-9} mm Hg at 25° C

Dissociation Constant: No dissociation from pH 1 to 9

Octanol/Water partition coefficient: Log P_{ow} = 3.769 at 25° C

pH: 6.29 at 24.3° C (1% aqueous dispersion)

Oxidizing or Reducing Action: None

Stability: Stable. No observed changes in test material

TOXICOLOGY CHARACTERISTICS

Action Herbicide

Acute Oral Toxicity (rats): LD50 Males and Females > 5,000 mg/kg
Toxicity Category: IV

Acute Dermal Toxicity (rats): LD50 > 2,000 mg/kg
Toxicity Category: III

Acute Inhalation Toxicity (rats): LC50 > 5.0 mg/L
Toxicity Category: IV

Primary Eye Irritation (rabbits): No irritation
Toxicity Category: IV

Primary Skin Irritation (rabbits): No dermal irritation
Toxicity Category: IV

Dermal Sensitization (guinea pigs): Non-sensitizer

Fluthiacet-Methyl-248757 Technical
(manufacturing use product)

Acute Oral Toxicity (rats): LD50 Males and Females > 5,000 mg/kg
Toxicity Category: IV

Acute Dermal Toxicity (rabbits): LD50 > 2,000 mg/kg
Toxicity Category: III

Acute Inhalation Toxicity (rats): LC50 > 5.0 mg/L
Toxicity Category: IV

Primary Eye Irritation (rabbits): Minimum eye irritant
Toxicity

Category:	III
Primary Skin Irritation (rabbits):	No dermal irritation
Toxicity Category:	IV
Dermal Sensitization (guinea pigs):	Non-sensitizer
Neurotoxicity screening battery (rat):	Negative at 2,000 mg/kg
90-day dietary (rats):	NOAEL = 100 ppm [6.19 mg/kg/day for males and 6.80 mg/kg/day for females] LOAEL = 3,500 ppm [216 mg/kg/day for males and 249 mg/kg/day for females] based on decreased body weight gains as well as effects on hematology, clinical chemistry, urinalysis parameters, liver weights and microscopic pathology.
6-week dietary (dog):	NOAEL = 6,500 ppm [236 mg/kg/day] for males and 2,000 ppm [77.7 mg/kg/day] for females LOAEL = 20,000 [709 mg/kg/day] for males and 6,500 ppm [232 mg/kg/day] for females based on decreased body weight gain.
28-day dermal (rats):	NOAEL = 1,000 mg/kg/day the highest dose tested [HDT].
Subchronic Neurotoxicity (rats):	Systemic NOAEL = 10 ppm [0.576 mg/kg/day] for males and 20,000 ppm [1,354 mg/kg/day],[HDT] in females. Systemic LOAEL = 10,000 [556 mg/kg/day] in males based on decreased body weight and food consumption. Neurotoxicity NOAEL = 20,000 ppm [1,128 mg/kg/day for males and 1,354 mg/kg/day for

	females], [HDT].
Developmental Toxicity (rabbit):	Maternal NOAEL = 1,000 mg/kg/day [HDT] Developmental NOAEL = 300 mg/kg/day Developmental LOAEL = 1,000 mg/kg/day based on a slight non-significant increased incidence of irregularly shaped sternebrae attributed to a delay in fetal development.
Developmental Toxicity (rat):	Maternal NOAEL and Developmental NOAEL = 1,000 mg/kg/day [HDT]
Two-Generation Reproduction (rat):	Parental Systemic NOAEL = 25 ppm [1.59 mg/kg/day for males and 1.73 mg/kg/day for females] Parental Systemic LOAEL = 500 ppm [31.8 mg/kg/day for males and 35.2 mg/kg/day for females] based on reduced male body weight gains and hepatic pathology. Reproductive NOAEL = 500 ppm [31.8 mg/kg/day for males and 37.1 mg/kg/day for females] Reproductive LOAEL = 5,000 ppm (313 mg/kg/day for males and 388 mg/kg/day for females) based on decreases in mean litter body weights.
1 Year Chronic Feeding (dog):	NOAEL = 2,000 ppm [57.6 mg/kg/day] in males and 1,000 ppm [30.3 mg/kg/day] for females LOAEL = 20,000 ppm [582 mg/kg/day] for males and 5,000 ppm [145 mg/kg/day] for females based on effects observed in the erythropoietic system and the liver.
Chronic Feeding/ Carcinogenicity (rat):	Systemic Toxicity NOAEL = 50 ppm [2.1 mg/kg/day in males and 2.5 mg/kg/day in females]. Systemic Toxicity LOAEL = 3,000 ppm [130 mg/kg/day in males and 154 mg/kg/day in females] based on decreased body weights, liver toxicity, pancreatic toxicity and

microcytic anemia in males; and liver toxicity, uterine toxicity and slight microcytic anemia in females. In males only at 3,000 and 5,000 ppm (130 and 219 mg/kg/day, respectively) there was an increase in the trend toward pancreatic exocrine adenomas and pancreatic islet cell adenomas.

Carcinogenicity (mouse): Systemic Toxicity NOAEL = 1 ppm [0.1 mg/kg/day in males and females] Systemic Toxicity LOAEL = 10 ppm [1.0 mg/kg/day in males and 1.2 mg/kg/day in females] based on non-neoplastic liver findings. In males at 100 and 300 ppm (10 and 32 mg/kg/day, respectively) there was an increase in the number of mice with hepatocellular adenomas, carcinomas and/or adenomas/carcinomas.

Carcinogenicity: The Health Effects Division Cancer Assessment Review Committee has classified Fluthiacet-methyl in accordance with the Agency's *Proposed Guidelines for Carcinogen Risk Assessment* (April 10, 1996) as a "likely to be a human carcinogen." Evidence for carcinogenicity was demonstrated by the presence of pancreatic tumors (exocrine adenomas, islet cell adenomas and combined islet cell adenomas + carcinomas) in male rats and liver tumors (adenomas and combined adenomas + carcinomas) in male and female mice. The Committee recommended a linear low-dose approach (Q_1*) for human characterization and determined that extrapolation should be based on the combined hepatocellular tumors (adenomas and carcinomas) in male mice.

Mutagenicity Fluthiacet-methyl was negative for mutagenic/genotoxic effects in bacterial or cultured mammalian cells and did not cause DNA damage in bacterial or primary rat hepatocytes. In vitro cytogenetic assays performed with two different mammalian cell lines demonstrated that fluthiacet-methyl is clastogenic both in the presence and absence of S9 activation. Although

the test substance is negative for micronuclei induction in mouse bone marrow, a significant increase in micronuclei is seen in stimulated rat liver cells following *in vivo* exposure.

Metabolism: Based on the results of the rat metabolism studies, fluthiacet-methyl was absorbed rapidly at both the low and high dose for both male and female rats. Repeated oral dosing had no effect on extent of absorption. Tissue levels of ^{14}C-fluthiacet-methyl derived radioactivity in the single and repeated low dose groups did not exceed 0.018 ppm for any tissue. At the single high dose, female rats showed higher levels of ^{14}C-fluthiacet-methyl derived radioactivity in tissues than males except for muscle, brain, fat and plasma. Excretion in males was predominantly in feces for all dose groups, with between 67-87% of administered radioactivity excreted by this route. In females, the percentage of administered radioactivity in urine across all dose groups (40-48%) was approximately equivalent to the percent excreted in feces (39-52%). The greater fecal excretion in males was based on a greater percentage excretion in bile for males (37%) vs. females (19%).

ECOLOGICAL CHARACTERISTICS

Avian Acute Toxicity:
- Bobwhite Quail: LD_{50} > 2250 mg/kg
- Mallard Duck: LD_{50} > 2250 mg/kg

Avian Dietary Toxicity:
- Bobwhite Quail: 5-day LC_{50} > 5620 ppm
- Mallard Duck: 5-day LC_{50} > 5620 ppm

Avian Reproduction:
- Bobwhite Quail*: No Observed Adverse Effect Concentration (NOAEC) = 100 ppm
  Lowest Observed Adverse Effect Concentration (LOAEC) > 100 ppm
- Mallard Duck*: NOAEC = 100 ppm
  LOAEC > 100 ppm

*Supplemental studies since No Observed Adverse Effect Concentration (NOAEC) was not determined.

Freshwater Fish Acute Toxicity:

Bluegill Sunfish	96-hour LC_{50} = 140 ppb
Rainbow Trout:	96-hour LC_{50} = 43 ppb

Freshwater Fish Early Life-Stage Toxicity:

Fathead Minnow	NOAEC = 2.7 ppb
	LOAEC = 6 ppb ai based on dry weight, wet weight and length
	MATC** = 4 ppb

** Defined as the geometric mean of the NOEC and LOEC

Freshwater Invertebrate Toxicity:

Daphnia magna	48-hour EC50 > 2.3*** ppm ai

***Solubility limit of the test material was reported to be 0.64 ppm

Freshwater Invertebrate Life-Cycle Toxicity:

Daphnia magna	NOAEC = 35 ppb
	LOAEC = 70 ppb based length
	MATC = 49 ppb

Estuarine/Marine Invertebrate Acute Toxicity

Eastern Oyster	96-hour LC_{50}/EC_{50} = 700 ppb
Mysid	96-hour LC_{50}/EC_{50} = 280 ppb

Non-Target Insects Toxicity:

Honey Bee	
Acute Contact	LD50 > 100 µg ai/bee - Technical

Seedling Emergence and Vegetative Vigor for Fluthiacet-methyl Technical (Tier II)

Seedling Emergence:

Monocot - Corn	EC_{25} > 0.18 (lb ai/acre) - none
Monocot - Oat	EC_{25} > 0.18 (lb ai/acre) - none
Monocot - Onion	EC_{25} = 0.010 (lb ai/acre) - dry weight
Monocot - Ryegrass	EC_{25} > 0.018 (lb ai/acre) - phytotoxicity
Dicot - Cabbage	EC_{25} > 0.018 (lb ai/acre) - none
Dicot - Cucumber	EC_{25} > 0.018 (lb ai/acre) - none
Dicot - Lettuce	EC_{25} > 0.018 (lb ai/acre) - none
Dicot - Radish	EC_{25} > 0.018 (lb ai/acre) - phytotoxicity
Dicot - Soybean	EC_{25} > 0.018 (lb ai/acre) - none
Dicot - Tomato	EC_{25} > 0.018 (lb ai/acre) - phytotoxicity

Vegetative Vigor

Monocot - Corn	EC_{25} > 0.18 (lb ai/acre) - none
Monocot - Oat	EC_{25} > 0.18 (lb ai/acre) - none
Monocot - Onion	EC_{25} = 0.010 (lb ai/acre) - dry weight
Monocot - Ryegrass	EC_{25} > 0.018 (lb ai/acre) - height
Dicot - Cabbage	EC_{25} = 0.0017 (lb ai/acre) - dry weight
Dicot - Cucumber	EC_{25} = 0.0008 (lb ai/acre) - dry weight
Dicot - Lettuce	EC_{25} = 0.0010 (lb ai/acre) - dry weight
Dicot - Radish	EC_{25} > 0.018 (lb ai/acre) - phytotoxicity
Dicot - Soybean	EC_{25} > 0.018 (lb ai/acre) - phytotoxicity
Dicot - Tomato	EC_{25} = 0.0012 (lb ai/acre) - dry weight

Non-target Aquatic Plant Toxicity (Tier II):

Vascular Plants

Duckweed	
Lemna gibba	EC_{50} = 2.2 ppb

Nonvascular Plants

Green algae	
*Kirchneria subcapitata**	EC_{50} = 2.51 ppb

Formerly Selenastrum capricornutum

Marine diatom	
Skeletonema costatum	EC_{50} = 5.13 ppb ai

Freshwater diatom	
Navicula pelliculosa	EC_{50} = 7.22 ppb

Blue-green algae	
Anabaena flos-aquae	EC_{50} > 18.4 ppb

Fluthiacet-methyl was shown to be practically non-toxic to birds, practically non-toxic to small mammals, practically non-toxic to bees and other beneficial insects, very highly toxic to fish, and moderately toxic to fresh water invertebrates. For seedling emergence, onion is the most sensitive non-target plant species and for vegetative, vigor, cucumber is the most sensitive non-target plant species. For aquatic plants, duckweed and nonvascular green algae are the most sensitive aquatic plant species.

There are no acute or chronic risk to non-target endangered fish, birds, aquatic invertebrates, terrestrial or aquatic plants

or endangered species. Risks to endangered terrestrial and aquatic species are expected to be minimal form the use of Action Herbicide on soybeans. Because surfactant is used with the end-use product, and may enhance the product's phytotoxicity, limited vegetative vigor test with onion, tomato, cucumber and an aquatic test with duckweed are a condition of the registration for Action Herbicide.

To reduce the risk to non-target species the following statements must appear in the Environmental Hazards section of the label of end use products:

> This pesticide is toxic to fish and aquatic invertebrates. Do not apply directly to water, or to areas where surface water is present or to intertidal areas below the mean high water mark. Drift and runoff may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water by disposal of waste waters.

The following statement must appear in the Environmental Hazards section of the label of end use products:

> This pesticide is toxic to fish and aquatic invertebrates. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans or other waters unless in accordance with the requirements of a National Pollutant Discharge Elimination System (NPDES) permit and the permitting authority has been notified in writing prior to discharge. Do not discharge effluent containing this product to sewer systems without previously notifying the sewage treatment plant authority. For guidance contact your State Water Board or Regional Office of the Environmental Protection Agency.

ENVIRONMENTAL CHARACTERISTICS

Fluthiacet-methyl in combination with its free acid equivalent was effectively stable against simple hydrolysis. Parent Fluthiacet-methyl and three degradates are not persistent to photodegradation in water with combined half-life to be 9.5 and 13.4 days respectively in two studies. On soil surfaces, parent fluthiacet-methyl and three degradates photolyzed with a half-life of 12.4 days.

Parent Fluthiacet-methyl and three degradates in aerobic soil degraded with a combined half-life of approximately 8 ± 3 days and 7 ± 4 days, respectively in two studies. Parent Fluthiacet-methyl and three degradates in anaerobic soil degraded with a combined half-life of approximately 10 ± 4 days in two studies.

Fluthiacet-methyl was determined to be very mobile in soils. Parent fluthiacet-methyl and three degradates had an effective or combined half-life of approximately 6 days. Although mobile, the transience of parent fluthiacet-methyl and its degradates means that the environmental exposure times and exposure concentrations relative to toxicity would be low.

Fluthiacet-methyl per se did not bioconcentrate in bluegill sunfish but numerous structurally related transformation products were identified. All residues combined in fish tissue were 20x, 450x and 300x for edible tissue, nonedible tissue and whole fish respectively. After 1 day in clean water, the level of combined residues in the edible tissue of fish dropped by 57%. After 14 days in clean water 82% of the combined residues in fish edible tissue had been eliminated. Because the parent and suite of degradates are relatively transient, and are present at levels that for purposes of bioconcentration are not considered to be meaningful, and because degradates are generally more polar than parent, significant bioconcentration would not be expected.

Based on GENEEC and SCI-GROW computer models, concentrations of fluthiacet-methyl in surface water and ground water are expected to be 0.3 µg/L and 0.002 µg/L, respectively.

Specific labeling for ground and surface water are not needed at this time.

TOLERANCE ASSESSMENT

Tolerances are established for residues of the herbicide, fluthiacet-methyl, acetic acid, [[2-chloro-4-fluoro-5-[(tetrahydro-3-oxo-1*H*,3*H*-[1,3,4]thiadiazolo[3,4-α]pyridazin-1-ylidene)amino]phenyl]thio]-methyl ester, in or on soybeans at 0.01 part per million (ppm).

AGGREGATE EXPOSURES

In examining aggregate exposure, Food Quality Protection Act (FQPA) directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures. The primary non-food sources of exposure the Agency looks at include drinking water (whether from groundwater or surface water), and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

1. From Food and Feed Uses

The chronic Reference Dose (RfD) for fluthiacet-methyl is 0.001 mg/kg/day. This value is based on the systemic NOAEL of 0.1 mg/kg/day in the mouse carcinogenicity study with a 100-fold uncertainty factor to account for interspecies extrapolation (10x) and intraspecies variability (10x).

In the prenatal developmental study with rabbits, *in utero* exposure did not result in maternal toxicity at 1,000 mg/kg/day. Developmental toxicity, however, was seen at this dose as a non-statistical increase in irregular sternebrae (an effect attributed to a delay in fetal development, a variation which is reversible). The occurrence of developmental toxicity at a dose at which no maternal toxicity was noted indicates an apparent susceptibility. EPA; however, determined that the apparent susceptibility is not convincing for the following reasons:

a) the increased incidence of irregular sternebrae was not statistically significant when compared to concurrent controls; b) the increase occurred primarily at the Limit-Dose (1,000 mg/kg/day); c) it was the only anomaly observed in the study (i.e., a single variation); d) the dose response was not strong since there was only a small increase in the litter incidences between the low-dose (5 mg/kg/day) and the high-dose (1,000 mg/kg/day), with the mid- and high-dose groups having 8 litters with this variation; and e) this endpoint is considered appropriate to establish a LOAEL, but not appropriate for risk assessments.

An extra safety factor to protect infants and children is not needed based on the following considerations:

(a) the available hazard assessment studies indicated no increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure to fluthiacet-methyl; and, (b) exposure assessments do not indicate a potential risk to infants and children based upon the very low application rates and quick dissipation of fluthiacet-methyl, the dietary exposure estimates use field study data which results in an overestimate of dietary exposure; modeling data are used for ground and surface source drinking water exposure assessments which result in estimates considered to be upper-bound concentrations; and there are no residential uses.

A DEEM chronic exposure analysis was conducted using tolerance levels for soybeans and assuming that 25 percent of the crop is treated to estimate dietary exposure for the general population and 22 subgroups. The chronic analysis showed that exposures from tolerance level residues in or on soybeans for non-nursing

infants less than 1 years old (the subgroup with the highest exposure) would be 0.6% of the Reference Dose (RfD). The exposure for the general U.S. population would be 0.1% of the RfD.

A lifetime dietary carcinogenicity exposure analysis was conducted for fluthiacet-methyl using the proposed tolerances along with the assumption of 25% of the crop treated and a Q* of 2.07×10^{-1} $(mg/kg/day)^{-1}$. A lifetime risk exposure analysis was also conducted using the DEEM computer analysis. The estimated cancer risk (2.06×10^{-7}) is less than the level that the Agency usually considers for negligible cancer risk estimates.

2. From Potable Water

Drinking water acute estimated concentrations (DWECs) for surface water was calculated by GENEEC computer models to be 0.3 parts per billion (ppb). The DWECs for ground water based on the computer model SCI-GROW were calculated to be an average of 0.002 ppb.

The drinking water level of comparisons (DWLOCs) for chronic exposure to fluthiacet-methyl in drinking water calculated for U.S. population was 35 ppb and for non-nursing infants less than 1 year old the DWLOC was 10 ppb. EPA's chronic drinking water level of comparison for the U.S. population and the subgroup of concern is above the estimated exposures for fluthiacet-methyl in water of 0.3 ppb for surface water and 0.002 ppb for groundwater.

A DWLOC for cancer was calculated as 0.133 ppb. The EEC in surface water and groundwater for fluthiacet-methyl are 0.1 ppb [0.3 ppb(the 56-day concentration)/3] and 0.002 ppb, respectively. The model exposure estimates are less than the cancer DWLOC.

EPA concludes that there is a reasonable certainty that no harm will result from aggregate exposure to fluthiacet-methyl residues. The nature of the residue in plants is adequately understood for the purposes of this tolerance. Based on the results of animal metabolism studies, it is unlikely that significant residues would occur in secondary animal commodities from this use.

3. From Non-Dietary Uses

There are no non-food uses of fluthiacet-methyl registered. No non-dietary exposures are expected for the general population.

4. Cumulative Exposure to Substances with Common Mechanism of Toxicity

Fluthiacet-methyl is structurally an imine chemical. For fluthiacet-methyl, EPA has not yet conducted a detailed review of common mechanisms to determine whether it is appropriate, or how to include this chemical in a cumulative risk assessment. After EPA develops a methodology to apply common mechanism of toxicity issues to risk assessments, the Agency will develop a process (either as part of the periodic review of pesticides or otherwise) to reexamine these tolerance decisions. The Agency has determined that there are no metabolites of toxicological concern associated with fluthiacet-methyl. Therefore, EPA has not assumed that fluthiacet-methyl has a common mechanism of toxicity with other substances.

EPA is required to develop a screening program to determine whether certain substances (including all pesticides and inerts) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or such other effect...." The Agency is currently working with interested stakeholders, including other government agencies, public interest groups, industry and research scientists in developing a screening and testing program and a priority setting scheme to implement this program. Congress has allowed 3 years from the passage of FQPA (August 3, 1999) to implement this program. At that time, EPA may require further testing of this active ingredient and end use products for endocrine disrupter effects.

OCCUPATIONAL EXPOSURE

Occupational risk assessments via dermal (short- and intermediate-term) and inhalation exposure routes were not required. A chronic non-cancer endpoint of 0.1 ppm was selected; however, based on use patterns (maximum of two applications per season at 0.0045 lb ai/A or one application at 0.007 lb. ai/A, chronic exposure is not expected.

A cancer occupational risk assessment was conducted and the base line total risk for occupational exposure was calculated to range from 6.6×10^{-7} to 6.5×10^{-8}. This is a level which the Agency generally considers to be acceptable for excess life-time occupational cancer risk.

SUMMARY OF DATA GAPS

1. Vegetative Vigor with onion, tomato, and cucumber conducted with Action Herbicide plus surfactant [Guideline

#123-1].

2. Aquatic Plant Growth with duckweed conducted with Action Herbicide plus surfactant [Guideline #123-2].

3. Improved Analytical Methods of two orders of magnitude for fluthiacet-methyl and degradates in soil and water.

PUBLIC INTEREST FINDING

Action Herbicide is effective at controlling certain broadleaf weeds that are common through out soybeans production areas, and is particularly effective in controlling velvetleaf. Due to lower use rates and the alternative herbicides, Pinnacle, Pursuit, Basagran and Resource, that will be replaced, the total herbicide volume applied to soybeans would be reduced.

GOVERNMENT PERFORMANCE AND RESULTS ACT (GPRA)

Registering fluthiacet-methyl will meet the objectives of GPRA title 3.1.1 by assuring new pesticides that enter the market are safe for humans and the environment and title 4.1.2 by reducing environmental exposure to herbicides.

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